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(54) Title: HALOTHERAPY METHOD

(57) **Abstract:** The invention relates to a convenient yet efficacious method of alleviating the severity or reducing the duration of respiratory ailments, especially the common cold or influenza. The method comprises administering to a person, over a period of from 1 to 14 days, by inhalation from a portable dispenser, one or more doses of sodium chloride, wherein the sodium chloride is in the form of an aerosol of 1 to 5 μm particles and each dose consists essentially of from 50 to 5000 μm sodium chloride, administered via from 2 to 200 inspirations. Suitable dispensers include self-milling dry powder dispensers and liquid nebulisers. Doses are preferably administered via a pulsed regimen comprising two or more periods of sodium chloride inhalation separated by periods of normal breathing. The invention further relates to the use of sodium chloride in the manufacture of a medicament for such methods.

Halotherapy Method

Field of the Invention

The present invention relates to a method of treating respiratory ailments, especially the common cold or influenza, with sodium chloride. The invention further relates to the use
5 of sodium chloride in the manufacture of a medicament for such methods.

Background

Treatment of respiratory diseases by inhalation of fine rock salt particles (halotherapy) in salt caves or salt mines has been practised for centuries in places such as Eastern Europe. The efficacy is associated with the unique micro climate within the salt caves and mines.
10 The main curative factor is an atmosphere containing dry sodium chloride aerosol with particles of 2 to 5 microns in size. The salt aerosol is formed by the convective diffusion of the fine salt particles from the salt walls. Halotherapy has been recognized as a highly effective drug-free treatment for patients with various forms of chronic nonspecific pulmonary diseases. In a typical treatment, a patient will reside in the salt caves for up to
15 twelve hours per day, breathing in the fine salt powder. In areas where salt mines are not available, special rooms (halochambers) have been constructed in which the environmental conditions of the salt mines are artificially reproduced. The patient resides in the halotherapy rooms in like manner as for the salt caves or mines.

Russian patent 209313 C1 describes a rehabilitation procedure for young children
20 suffering from frequent respiratory infections whereby they have repeat daily exposures to halochamber conditions, the exposure building up from 5 minutes to 20 minutes per session.

Halochambers are not generally available for most people so that there has been a need for more convenient apparatus. SU1793932 describes a salt grinder in an enclosed
25 chamber with an air input and output for generating salt aerosols for respiratory treatment in a separate treatment chamber. More recently, WO 98/48875 disclosed a portable dispenser capable of producing particles of from 5 to 20 μm , and hence targeted at the upper portion of the lower respiratory tract, for the treatment of cold symptoms.

Nevertheless, there remains a need for improved methods for halotherapy which are both convenient to use i.e., for personal use, without the aid of cumbersome equipment or equipment which requires technician or other assistance to operate, and which make effective interventions in the course of respiratory ailments.

- 5 It has now been found that short periods of repeat inhalations of salt aerosols generated from a hand-held, portable device can deliver clinically significant improvements in the severity and duration of symptoms, such as cough, runny nose and sore throat, associated with the common cold or influenza.

Summary of the Invention

- 10 A method of treating respiratory ailments of a person comprising administering to the person, over a period of from 1 to 14 days, by inhalation from a portable dispenser, one or more doses of sodium chloride, wherein:
- a) the sodium chloride is in the form of an aerosol of particles having a mean size in the range of from 1 to below 6 μm ;
 - 15 b) each dose consists essentially of from 50 to 10,000 μg sodium chloride;
 - c) each dose is administered via from 2 to 200 inspirations.

Suitable dispensers include self-milling dry powder dispensers and liquid nebulisers. Doses are preferably administered via a pulsed regimen comprising two or more periods of sodium chloride inhalation separated by periods of normal breathing. The invention
20 further relates to the use of sodium chloride in the manufacture of a medicament for such methods.

Detailed Description of the Invention

The methods and uses herein relate to the treatment of respiratory ailments, especially to treatment of the common cold and influenza and symptoms associated therewith such as
25 runny nose, cough and sore throat. In particular, the invention relates to treatment of the common cold and its symptoms.

The period of treatment is for a period of from about one to about fourteen days, preferably for about one to about seven days and more preferably for about three to about

seven days. Best results are obtained with daily treatment but beneficial results can still be obtained if some treatment days are missed.

Whilst the mechanism of action is not clearly understood it appears that best results are obtained with mean particle sizes which are suitable for deep lung delivery. These are generally in the range of from about 1 to about below 6 μm , preferably from about 1 to about 5 μm , and more preferably from about 2 to about 5 μm .

A dose can be delivered by the user breathing in an aerosol of the particles generated by the dispenser. Each dose consists essentially of from about 50 to about 10,000 μg , preferably from about 100 to about 5000 μg , and more preferably about 500 μg of sodium chloride. Weights refer to the sodium chloride on a 100% active basis. By 'consists essentially of' is meant that the sodium chloride is the primary active. Excipients and other co-actives in lesser amounts can be used. In particular, excipients may be added to sodium chloride powder to improve dispensing properties or to prevent agglomeration. An example is lactose. Lactose is typically added for this purpose in the range of 2 to 5 percent. Since, at the amounts administered, the sodium chloride can not normally be sensorially detected, it is preferred to add other ingredients to provide an organoleptic signal so that the user can be reassured that the dispenser is actually working. Preferred organoleptic ingredients are selected from flavours and physiological coolants, such as menthol. Such ingredients are typically added such that they have a proportion by weight less than about 10 percent.

The sodium chloride can be in the form of a dry powder or an aqueous solution. Dry powder forms are preferred. A suitable dispenser for dry powder delivery is disclosed in commonly assigned co-pending patent application whose US serial no. is 09/479 968, filed 10 January 2000, which is incorporated herein by reference in its entirety. The afore-mentioned dispenser includes a means for milling a dry, bulk sodium chloride source and a cyclone for selecting the desired particle size fraction. This device overcomes the problem of moisture-induced salt agglomeration which is inherent to devices employing pre-milled sodium chloride. Accordingly, a preferred dispenser comprises means for milling the sodium chloride doses on demand from a bulk sodium chloride supply. The dispenser can be loaded with a granular sodium chloride source and

will then mill to produce the required fraction. Volume output can be controlled by e.g. adjustment of motor speed and blade configuration. The dispenser can be calibrated by running it for several minutes and determining the weight loss at each minute interval. Particle size can be checked by using a vacuum to suck the particles from the output line of the dispenser the laser beam of Malvern Mastersizer X equipment. Distance from the lens for this measurement is normally set at 25cm.

A suitable dispenser for aqueous solution delivery is a portable liquid nebuliser, for example as taught in WO92/11050 from Omron Corp. A commercial device is sold in Europe under the name 'Omron U1' by Omron Healthcare GmbH. The Omron device uses a vibrating disc to dispense liquid through a 3 μm pore mesh. PCT application WO 93/10910, from The Technology Partnership Limited also uses a mechanically oscillating membrane to dispense liquid through a mesh in order to generate particles. A preferred dispenser for sodium chloride doses in the form of an aqueous solution is a liquid nebuliser comprising a mesh having a screen size of from 1 to 3 μm .

In order for delivery to be efficient it is preferred that when the sodium chloride dose is in the form of an aqueous solution, that it has a sodium chloride concentration of above isotonic solution level ($\sim 0.9\%$), preferably from 1.5% to 10%, more preferably from 2% to 7% and especially about 4%.

Irrespective of the precise dose form, each dose is administered via from about 2 to about 200, preferably from about 5 to about 100 and more preferably from about 10 to about 80 inspirations. It is preferred that each inspiration is a deep breath, that is preferred that each inspiration inhales at least about 0.5 litres of air, preferably at least about 1 litres, and lasts for at least 1s. Prolonged deep breathing can be tiring, especially when a person is already suffering from a respiratory ailment. In a preferred inhalation regimen, each dose is administered via a pulsed regimen comprising two or more periods of sodium chloride inhalation separated by rest periods of normal breathing.

Example

A dispenser according to Figures 1-2 and Example 1 of US patent application serial no. 09/479 968, incorporated herein by reference, is loaded with granular sodium chloride (Riedel-de Haen 13423, meeting analytical specification of DAB, Ph. Eur., BP, Ph.

Franc.,USP.) having a typical diameter of about 300 to 400 μm . The impeller is set to rotate at about 3000 rpm. Sodium chloride particles between 2 to 5 μm have sufficiently low inertia as to be classified and carried by the exiting stream through the conduit. When the chamber initially contains 1 gram of sodium chloride, approximately 1000 μg per minute of fine particles are dispensed. Over 99% of the particles dispensed are between 2 to below 6 μm . The device may need to be primed by running it for a few minutes before first treatment. Once primed then the volume output is about constant on repeated use.

A mouthpiece attached to the exit conduit allows a person suffering from the common cold to take deep breaths from the device thereby inhaling the salt particles. Treatment is continued for 10 minutes, with the person inhaling for about half of that period and taking a rest period of one minute after every third minute. The treatment is repeated over a period of from 5 to 7 days. In a controlled clinical test using these conditions, the duration of the symptoms of sore throat, runny nose and cough was reduced from an average of about 8 days to an average of 5 to 6 days, relative to placebo (air). The severity of the same symptoms was also significantly reduced during the time that they were experienced.

WHAT IS CLAIMED IS:

1. A method of treating respiratory ailments of a person comprising administering to the person, over a period of from 1 to 14 days, by inhalation from a portable dispenser, one or more doses of sodium chloride, wherein:
 - 5 a) the sodium chloride is in the form of an aerosol of particles having a mean size in the range of from 1 to below 6 μm ;
 - b) each dose consists essentially of from 50 to 10,000 μg sodium chloride;
 - c) each dose is administered via from 2 to 200 inspirations.
2. The method of Claim 1 wherein each dose comprises dry sodium chloride powder.
- 10 3. The method of Claim 1 wherein each dose comprises an aqueous sodium chloride solution having a sodium chloride concentration of at least 10%.
4. The method of Claim 1 or Claim 2 wherein each dose further comprises an ingredient to provide an organoleptic signal, the ingredient preferably being selected from flavours and physiological coolants.
- 15 5. The method of any preceding claim wherein each dose is from 100 to 5000 μg .
6. The method of Claim 1 or Claim 2 wherein the dispenser comprises means for milling the doses on demand from a bulk sodium chloride supply.
7. The method of Claim 3 wherein the dispenser is a liquid nebuliser comprising a mesh having a screen size of from 1 to 3 μm .
- 20 8. The method of any preceding claim wherein the ailment is the common cold.
9. The method of Claim 8 for reducing the duration of the cold.
10. The method of any of Claims 1 to 7 wherein the ailment is influenza.
11. The method of any preceding claim wherein each dose is administered over a total inhalation time period of from 10 to 1000s.
- 25 12. The method of any preceding claim wherein each dose is administered via a pulsed regimen comprising two or more periods of sodium chloride inhalation separated by rest periods of normal breathing.

13. The method of any preceding claim wherein each inspiration exchanges at least 0.5 litres of air and lasts for at least 1s.
 14. The use of sodium chloride in the manufacture of a medicament for treating respiratory ailments, the treatment comprising a method according to any of the preceding claims.
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